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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,024	06/24/2003	Bradley G. Thompson	16596-001001	7648

26176 7590 04/19/2007
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EXAMINER	
LI, BAO Q	
ART UNIT	PAPER NUMBER
1648	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/602,024	THOMPSON ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/18/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

RCE

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 02/20/2007 has been entered. An action on the RCE follows.

Response to Amendment

This is a response to the amendment filed on 2/20/07. Claim 34 has been amended. Claims 34-43 are pending before the examiner.

1. Claims 34-43 are still rejected under 35 U.S.C. 112, first paragraph on the same ground as stated in the previous office action.

2. Applicants traverse the rejection and submit that the claimed method provides at least two oncolyticc viruses, wherein each oncolytic virus selectively replicates in neoplastic cells having a phenotype selected from the group consisting of ras pathway activation, interferon.-resistance, p53-deficiency and Rb.-deficiency. Further, each of the at least two oncolytlc viruses replicates in neoplastic ceils having a different phenotype. Thus. for example, one oncolytic virus replicates in neoplastic cells with an interference-resistance phenotype, wherein the other oncolytic virus replicate in neoplastic cells with an Rb-deficiency phenotype. The claimed method also includes the use of conditions, which allow each oncolytic virus to selectively replicate in the neoplastic cells having the phenotype for which each oncolytic virus is specific.

3. In response to the examiner question cited in the previous office action, if both oncolytic viruses, such as herpes virus G207 and adenovirus ONYX, can replicate in either ras and/or p53 mutated neoplasm, applicants have amended claims as "each of the at least two oncolytic viruses replicates in newoplastic cells having a different phenotype." Applicants asserted that in this way, the claimed method could be performed in view other available technique for determining virus replication in the art.

4. Applicants' argument and amendment have been respectfully considered; however, it is still unpersuasive to overcome the rejection.

5. First, the amended claim 34 is still considered to be inoperable. Because when a phenotype of the neoplasm is unknown, how the claimed method cites to use each of at least two oncolytic viruses replicate in neoplastic cell having a different phenotype when the phenotype is simply still unknown. Moreover, as it is stated in the previous office action, lots of oncolytic viruses can be replicate in more then one phenotypic mutated neoplasm, and lots of cancers have more than one phenotypic mutations. In this condition, although the method of detecting virus replication and measurement of tumor or cancer development are well known, it is still undue experimentation to determine which phenotype(s) of the neoplasm has.

6. For example, a neoplasm having a ras mutation, it also has a defect interferon response pathway. In this case, reovirus, VSV and oncolytic HSV with λ345 gene mutation or oncolytic adenovirus lacking the gene encoding AVI and many more oncolytic virus can all replicate and kill the neoplasm. In this case, all theses oncolytic viruses can replicate in mote than one phenotypic neoplasm. Moreover, many kinds of tumors may contain more than phenotypes of oncogenes' mutations as evidenced by Einspahra et al. (Cancer Epidemiol. Biomarkers Prev. 2006, Vol. 15(8), pp. 1443-1450) cited in the previous office action. Einspahra et al. teach that both Ki-ras and p53 gene mutations occur with sporadic colorectal adenoma (Please see 1443, 1449 and Table 6). Still further, one oncolytic virus naturally can replicate in more than one phenotypes of neoplastic cells (Please see Smith et al. Exp. Opin. Invest. Drugs 2000, Vol. 9, No. 2, pp. 311-327, Table 2). If both viruses are admitted into a neoplasm that has both ras and p53 mutation, viruses will replicate well in the cancer cells and lead the cancer cells death, how you can determine which phenotype of the neoplasm is.

7. The specification does not provide sufficient evidence to support the claimed invention. In fact, the specification only provides one example of using reovirus to infect a biopsy tissue of breast cancer patient. Because the reovirus replicates in the tissue, applicants conclude that the breast cancer has a ras mutation. But there is other example how to test a neoplasm if the neoplasm has more than one or two kinds of proto-oncogens mutations. In fact, it is well known in the art both ral and ras oncogenes can prefer the reovirus replication in the neoplasm. Moreover, alteration of PKR pathway is not only cause by Ras mutation either.

8. Therefore, absence more evidence and guidance showing how to use ooncolytic viruses only can make a correct diagnosis of a phenotype of a neoplasm, it is still conclude that the undue experimentation would have been required for a person skilled in the art to make and use the claimed invention.

9. To this context, the rejection is still maintained.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Baoqun Li

BAOQUN LI, MD
PATENT EXAMINER

Bao Qun Li
April 14, 2007